Claims

1. An oral pharmaceutical dosage form comprising a core material that contains a proton pump inhibitor, one or more alkaline reacting compound(s) and optionally pharmaceutically acceptable excipients having a water soluble separating layer and an enteric coating layer characterized in that the core material is alkaline reacting and that the separating layer is being formed in situ during the enteric coating as a water soluble salt between the enteric coating layer polymer(s) and the alkaline reacting compound(s).

2. A dosage form according to claim 1, wherein the alkaline reacting compounds are selected from the group of alkaline organic substances, hydroxides of alkali metals or one of their alkaline salts of phosphoric acid, carbonic acid or silicic acid, or an alkaline ammonium salt.

3. A dosage form according to claim 2, wherein the alkaline reacting substance is a hydroxide of an alkali metal or an alkaline salt of phosphoric acid, carbonic acid or silicic acid, or an alkaline ammonium salt.

4. A dosage form according to claim 2, wherein the alkaline reacting compound is an alkaline organic substance, e.g. an amino acid or a salt thereof, an alkaline amine or a derivative thereof, or an alkaline salt of a weak organic acid.

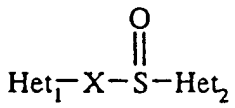
5. A dosage form according to claim 2, wherein the alkaline organic substance is an amino acid, e.g. lysine, arginine, ornitine or histidine, or an alkaline amine or a derivative thereof, e.g. N-methyl-D-glucamine or trometamine.

6. A dosage form according to claim 1, wherein the alkaline reacting compounds are present in a concentration of more than 0.1 mmol/g dry ingredients in the alkaline part of the core material.

7. A dosage form according to claim 1, wherein the enteric coating polymer(s) is/are hydroxypropyl cellulose derivative(s), e.g. hydroxypropylmethylcellulose acetate succinate.

8. A dosage form according to claim 1, wherein the enteric coating polymer is copolymerized methacrylic acid/methacrylic acid methyl esters.

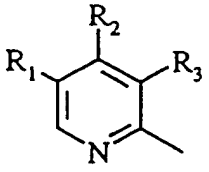
9. A dosage form according to claim 1, wherein the proton pump inhibitor is a compound of the general formula I or a pharmaceutically acceptable salt thereof or a pure enantiomer thereof in neutral form or in the form of an alkaline salt



I

wherein

Het_1 is



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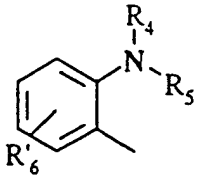

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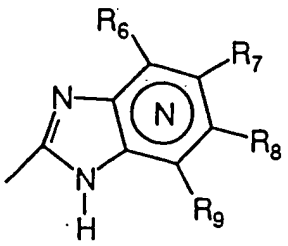

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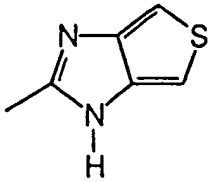

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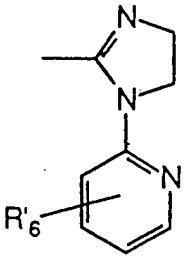

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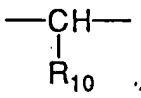

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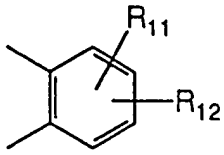

wherein

N in the benzimidazole moiety means that one of the carbon atoms substituted by R_6-R_9 optionally may be exchanged for a nitrogen atom without any substituents;

R_1, R_2 and R_3 are the same or different and selected from hydrogen, alkyl, alkoxy optionally substituted by fluorine, alkylthio, alkoxyalkoxy, dialkylamino, piperidino, morpholino, halogen, phenyl and phenylalkoxy;

R_4 and R_5 are the same or different and selected from hydrogen, alkyl and aralkyl;

R'_6 is hydrogen, halogen, trifluoromethyl, alkyl and alkoxy;

R_6-R_9 are the same or different and selected from hydrogen, alkyl, alkoxy, halogen, halo-alkoxy, alkylcarbonyl, alkoxycarbonyl, oxazolyl, trifluoroalkyl, or adjacent groups R_6-R_9 form ring structures which may be further substituted;

R_{10} is hydrogen or forms an alkylene chain together with R_3 and

R_{11} and R_{12} are the same or different and selected from hydrogen, halogen or alkyl and alkyl groups, alkoxy groups and moities thereof may be branched and straight C_1-C_9 -chains or comprise cyclic alkyl groups, for example cycloalkylalkyl.

10. A dosage form according to claim 1, wherein the proton pump inhibitor is omeprazole or an alkaline salt thereof.

11. A dosage form according to claim 1, wherein the proton pump inhibitor is a pure enantiomer of omeprazole or an alkaline salt thereof.

12. A dosage form according to claim 1, wherein the proton pump inhibitor is lansoprazole, one of its pure enantiomers or a pharmaceutically acceptable salt thereof.

13. A dosage form according to claim 1, wherein the proton pump inhibitor is pantoprazole, one of its pure enantiomers or a pharmaceutically acceptable salt thereof.

14. A dosage form according to claim 1, wherein the alkaline reacting core material is individual pellets intended for a capsule formulation or a tableted multiple unit dosage form.

15. A dosage form according to claim 1, wherein the alkaline reacting core material is a tablet.

16. A dosage form according to claim 1, wherein individually enteric coated pellets are compressed into a tableted multiple unit dosage form.

17. A process for the preparation of an oral, enteric coated pharmaceutical dosage form comprising a core material that contains a proton pump inhibitor, one or more alkaline reacting compounds and optionally pharmaceutically acceptable excipients having a water

soluble separating layer and an enteric coating layer characterized in that an alkaline reacting core material is prepared and coated with an enteric coating polymer wherein a separating layer between the core material and the enteric coating layer is formed in situ by a reaction between the enteric coating polymer(s) and the alkaline reacting compound(s) in the core material during the application of the enteric coating onto the alkaline reacting core material.

18. An oral, pharmaceutical dosage form comprising a proton pump inhibitor as defined in any of claims 1-16 for use in inhibiting gastric acid secretion in mammals and man.

19. A method for inhibiting gastric acid secretion in mammals and man by administering to a host in need thereof a dosage form comprising a therapeutically effective dose of a proton pump inhibitor as defined in any of claims 1-16.

20. Use of an oral pharmaceutical dosage form defined in any of claims 1 - 16 for the manufacture of a medicament useful in the treatment of gastric acid related diseases.